UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

08/846933

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/846,933	04/30/97	CLELAND	J [illegible]25BC3

EXAMINER

HM12/1014

EMILY M. HALIDAY
MCCUTCHEN, DOYLE, BROWN & EMERSEN, LLP
THREE EMBARCADERO CENTER
SAN FRANCISCO CA 94111

ART UNIT	PAPER NUMBER
RYAN, V	17

DATE MAILED:

10/14/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 7/22/99

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1, 4-9, 23-27 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1, 4-9, 23-27 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 16
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

SEE OFFICE ACTION ON THE FOLLOWING PAGES

DETAILED ACTION

The text of those sections of U.S. Code not included in this Office Action can be found in a prior Office Action.

The Examiner acknowledges receipt of the amendment filed July 22, 1999.

In this application:

Claim 1 was amended.

Claims 1, 4-9, and 23-27 are now pending and under examination.

Response to Amendment

(1) The objections to the drawings are maintained for reasons of record.

(2) The rejection of claims 1, 4-9, and 23-27 under 35 U.S.C. 112, first paragraph is maintained.

(3) The rejection of claims 1, 4-9 and 23-27 under 35 U.S.C. 103 as being unpatentable by Sanders et al in view of Eldridge et al (Mol Immunol) and further in view of Jeffery et al is maintained.

Applicant asserts that Sanders et al fail to teach triphasic release wherein specific percentages of the agent are released during specific phases of release.

Sanders et al provides a triphasic composition that falls within the scope of the claimed invention. The use of the antigen is taught by Eldridge et al who teach that antigens can be encapsulated into microspheres and given as vaccines which can be formulated to release in minimally two phases and as many as four phases. (See especially page 293, Discussion)

It is the Examiner's position that Sanders et al teach triphasic release. Note Figure 2 where a release is at day 1, a second release comes later. Note the percentage of antigen remaining at injection site is depicted to be approximately 75%. Thus, it would appear that at the first phase, Sanders triphasic microsphere released about 30% of the antigen. Sanders et al indicate further release is over 90 days. This would encompass the 2nd phase "wherein antigen is released over a period of 30 to 180 days." Although Sanders et al is silent regarding further release over 120 to 180 days, it is noted that Eldridge et al teach and suggest "using a combination of variables, at least a four discrete release of antigens can be achieved over a 120 day period and even over a period in excess of 1 year." (See page 293 of Eldridge)

Therefore, it would appear that Sanders et al teach the inventive concept of a triphasic release microsphere where the

antigen is released over a period that is encompassed by the Applicant's claims.

(4) The rejection of claims 5-7 under 35 U.S.C. 103 as being unpatentable by Sanders et al, Eldridge et al, and Jeffery et al (as applied to claims 1, 4, 9 and 23-27) and further in view of Wang et al is maintained for reasons of record.

(5) The rejection of claim 8 under 35 U.S.C. 103 as being unpatentable by Sanders et al, Eldridge et al, and Jeffery et al (as applied to claims 1, 4, 9 and 23-27) and further in view of Newman et al is maintained for reasons of record.

(6) The objection to claim 1 for informalities is withdrawn.

(7) The rejection of claims 1, 4-9 and 23-27 under 35 U.S.C. 112, first paragraph is maintained.

(8) The rejection of claims 1, 4-9 and 23-27 under 35 U.S.C. 112, second paragraph is withdrawn.

(9) The rejection of claims 1, 4, 9, and 23-27 under 35 U.S.C. 103 as being unpatentable by Floy et al is maintained.

Applicant asserts that Floy et al established the focus on continuous release systems. Applicant submits that the only teachings regarding multiphasic release suggest only that it might be possible to achieve a particular profile by combining two or more types of polymers. Moreover, Applicant contends that

the invention is based on a "strategy of manipulating at least 10 different parameters to produce a microsphere population having a desired multiphasic release profile" which was not taught by any of the prior art references.

Floy teach the PLGA system for administering peptides, proteins and drugs. While the reference does not teach the parameters recited in the claims, the reference acknowledges that the drug release profiles from the system typically exhibit a triphasic release profile. Moreover, the reference indicates that the copolymer ratio, device geometry, molecular weight and intrinsic viscosity influence the biodegradation and release profile of the polymer, and the parameters can be varied for optimization of the delivery system. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See In re Aller, 220 F.2d 454, 105 USPQ 322,325 (CCPA 1955).

Therefore, it would appear that Floy et al teach the inventive concept of a triphasic release system that is encompassed by the Applicant's claims.

(10) The rejection of claims 5-7 under 35 U.S.C. 103 as being unpatentable by Floy et al (as applied to claims 1, 4, 9 and 23-

27) in view of Immunization Practices Advisory Committee is maintained for reasons of record.

(11) The rejection of claim 8 under 35 U.S.C. 103 as being unpatentable by Floy et al in view of Immunization Practices Advisory Committee and further in view of Newman et al is maintained for reasons of record.

Applicant's arguments filed July 22, 1999 have been fully considered and they are not deemed to be persuasive regarding those rejections which are maintained.

(a) The rejection of claims 1, 4-9, and 23-27 under 35 U.S.C. 112, first paragraph is maintained.

Applicant maintains that *ipsis verbis* support for the term "beginning at the completion of" is not necessary, and sufficient support is demonstrated at page 5, lines 30-32.

Although pages 5-6 and Figure 8 discuss and demonstrate the phases of release, these sites do not teach or suggest the phases "beginning at the completion of" the previous phase. The specification does not convey with reasonable clarity to those skilled in the art that, as of the filing date sought, the inventors listed on the instant application were in possession of the presently claimed invention. The subject matter of the

claims need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. However, the claims now include information that was not provided in the original disclosure. In view of the above, the specification is viewed as failing to provide adequate written description or support for the presently claimed invention.

(b) The rejection of claims 1, 4-9 and 23-27 under 35 U.S.C. 112, first paragraph is maintained.

Applicant asserts support for the term "1 milliliter of aqueous antigen per 3 gram of polymer or less" and the release of microspheres over a period of "about 1 to 2 days".

The subject matter of the claims need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. However, the claims now include information that was not provided in the original disclosure. Applicant refers to page 16, line 29 to page 17, line 8 to demonstrate support for "1 milliliter of aqueous antigen per 3 gram of polymer or less". However, the specification the PLGA "is first dissolved in an organic solvent such as methylene chloride, or ethyl acetate with or without benzyl alcohol or acetone to the desired concentration (generally

about 0.05 to 1.0 g/mL, preferably about 0.3 to 0.6 g/mL)." This statement does not provide support for an antigen concentration of "1 milliliter of aqueous antigen per 3 gram of polymer or less".

Applicant asserts that, by studying Figure 8, one skilled in the art would believe the initial burst ends after about 2 days or release because the percent cumulative release jumps to 20% in the first two days of release and then abruptly levels off.

Figure 8, which is a graph demonstrating in vitro release of an antigen from PLGA microspheres, indicates the daily and cumulative percent release of antigen over a period of 120 days. However, it is not possible to determine what percent was released over a period of one to two days.

The following are new grounds of rejections:

Specification

Claim 1 is objected to because of the following informalities:

Claim 1, lines 7 and 10, where "about about" should be --about--.

Appropriate correction is required.

It is also noted that claim 1 was not properly amended. The claim was amended on February 22, 1999 to recite "the PLGA

polymer has a ratio of lactide to glycolide ranging from from about 100:0 to 50:50 weight percent". However, the claim as amended on July 22, 1999 does not accurately show the previous recitation.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

The Group and/or Art Unit location of your application in the Patent and Trademark Office may have changed. To aid in correlating any papers for this application, all further

correspondence regarding this application should be directed to Group Art Unit 1641.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to V. Ryan whose telephone number is (703)305-6558.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Papers related to this application may be submitted to the Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Art Unit 1641 is (703)308-4242.

V. Ryan
Patent Examiner/Art Unit 1641
October 1999
Ryan/vr

James C. Housel
JAMES C. HOUSEL 10/12/99
SUPERVISORY PATENT EXAMINER